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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAWLINGS, STEPHEN L 15	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/805,177	RODEN ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *1-40 and 42-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-45* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,7* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *14* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The election filed September 3, 2002 in Paper No. 10 and the supplemental election filed December 18, 2002 in Paper No. 12 are acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-45 are pending in the application. Claims 1-40 and 42-45 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Claim 41, insofar as the claim is drawn to a method for screening for cancer comprising determining the presence of antibodies specific for ATP-dependent iron transporter ABC-7, is currently under prosecution.

Drawings

4. The proposed substitute drawings filed October 2, 2001 in Paper No. 5 are acknowledged, but have been disapproved because Figure 12 has been improperly altered in lack of accordance with MPEP § 608.02(p). 37 CFR § 1.121 states: Any change to the application drawings must be submitted on a separate paper showing the proposed changes in red for approval by the examiner.

In addition, the proposed substitute of Figure 12 depicts the amino acid sequence of a protein, which is not identified by a sequence identification number and which is not included in the sequence listing. Therefore, acceptance of the proposed substitute drawings would have placed this application in non-compliance with the sequence rules set forth under 37 CFR §§ 1.821-1.825. Applicant is advised that should the proposed alterations to Figure 12 be made, substitute paper and computer-readable copies of the sequence of listing should be submitted together with a statement that both copies are the same and that no new matter has been introduced.

Furthermore, upon acceptance of the proposed substitute of Figure 12, the specification would be objected to because according to the brief description of the figures on page 10, the sequence depicted is SEQ ID NO: 1. Since the proposed substitute of Figure 12 depicts two sequences, the corresponding description would be incomplete and moreover it would be unclear which of the depicted sequences is SEQ ID NO: 1.

Specification

5. The disclosure is objected to because the disclosure refers to embedded hyperlinks and/or other forms of browser-executable code, which are impermissible and require deletion. See page 22, for example.

The attempt to incorporate essential or non-essential subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP § 608.01(p), paragraph I regarding incorporation by reference.

6. The specification is objected to because the use of numerous improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Examples of improperly used trademarks are found on pages 33, 39, and 47.

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

7. The specification is objected to because of the omission of the ATCC deposit number(s) throughout.

Claim Objections

8. Claim 41 is objected to because the claim is alternatively drawn to the subject matter of non-elected inventions.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 41 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The teachings of the specification are insufficient to enable the skilled artisan to use the claimed invention with a reasonable expectation of success without having the need to perform additional and an undue amount of experimentation. Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of

direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The specification does not exemplify the use of the claimed invention, but teaches, "the clinical significance of detection of autologous anti-tumor antibodies requires further analysis and must be assessed for each antigen" (page 4). While the specification teaches that the serum of a patient having ovarian serous carcinoma contains antibodies that bind the ATP-binding cassette 7 transporter (ABC-7), a protein that has been described by Allikmets, et al and has the amino acid sequence set forth under GenBank accession number AF133659, the specification does not teach that the sera of patients having ovarian cancer similarly contain antibodies that bind ABC-7. Moreover, the specification does not teach that the sera of patients having other types of cancer similarly contain such autoantibodies.

While Applicants' disclosed discovery appears to be novel, no factual evidence has been disclosed to support the assertion that the claimed invention can be used to ascertain the likelihood that an individual has cancer. As the specification teaches, the clinical significance of the discovery of the presence of anti-ABC-7 antibodies in the serum of a patient having cancer must be assessed, and it appears that the necessary further analysis has not been performed.

Nevertheless, the utility of autoantibodies that bind other tumor-associated antigens has been contemplated in the art. For example, the diagnostic and prognostic significance of finding antibodies in the sera of cancer patients that bind p53 has been carefully examined. While the finding may have value in some incidences, it has none in other incidences. Creaney, et al (*British Journal of Cancer* 84: 52-56, 2001) teach, "[t]he occurrence of anti-p53 antibodies does not serve as either a useful prognostic or diagnostic indicator in MM [malignant mesothelioma]" (abstract). Mack, et al (Oncological Reports 7: 669-674, 2000) reported that although the status of anti-p53 antibody is prognostically useful in managing patients with non-small cell lung cancer, statistical analysis of survival shows no correlation with the presence of anti-p53

antibodies in patients diagnosed with small cell lung cancer. Gadducci, et al (*Gynecol. Oncol.* **72**: 76-81, 1999) found that the presence of antibodies against p53 in the serum of patients having ovarian cancer had no prognostic relevance, concluding, "the assessment of preoperative serum anti-p53 antibodies seems to have a limited clinical value in the management of patients with advanced epithelial ovarian cancer" (abstract). Thus, it seems that the skilled artisan could not predict the utility of Applicants' disclosed discovery without having the need to first perform additional and an undue amount of experimentation to assess the clinical significance of the discovery of a patient having antibodies that bind ABC-7.

Tockman, et al (*Cancer Research* **52** (No. 9 supplement): 2711s-2718s, 1992) teach considerations necessary in bringing a cancer biomarker (intermediate endpoint marker) to successful clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to diagnosis and prognosis of ovarian cancer, or of any cancer. Tockman, et al teach that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence, and confirm marker predictive value in prospective population trials (abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and **if validated** can be used for population screening (page 2713, column 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and link those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate endpoint marker (page 2714, column 1). Clearly, prior to the successful application of newly described markers, these must be validated against acknowledged disease end points; and, the marker predictive value must be confirmed in prospective population trials (page 2716, column 2).

11. Claim 41 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification teaches that an isolated nucleic acid molecule encoding a protein that is specifically reactive with the immune serum of a patient diagnosed with ovarian cancer is "the ABC-7 ATP-dependent iron transporter (consistent with the sequence of gb|AF133659|AF133659)" (page 34). Allikmets, et al published the sequence of GenBank accession number AF133659. Claim 41 is drawn to a method comprising determining the presence of antibodies that bind the "ATP-dependent iron transporter ABC-7". Therefore, the claim encompasses a method comprising determining the presence of antibodies that bind any protein designated as such, including isoforms or variants of the protein described by Allikmets, et al, which have not been described in the specification. Accordingly, the specification is insufficient to meet the written description requirements set forth under 35 USC § 112, first paragraph.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

There is factual evidence to support this ground of rejection. The sequence of GenBank accession number BC006323 is defined as the complete coding sequence of human "ATP-binding cassette, sub-family B (MDR/TAP), member 7". Therefore, it appears that the protein having this sequence is appropriately deemed the same as the "ATP-dependent iron transporter ABC-7" to which claim 41 refers, but the specification clearly does not describe this protein. In addition, given the description of the "ATP-dependent iron transporter ABC-7" to which claim 41 refers, the skilled artisan could not envision, recognize, or predict the structure of at least a reasonable number of the proteins that are variants of the polypeptide described by Allikmets, et al.

The *Guidelines* state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an

adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 is vague and indefinite because the claim recites the term "increased likelihood". Because the specification does not define the term, the metes and bounds of the invention cannot be reasonably determined, as it cannot be ascertained what probability constitutes "an increased likelihood".

Conclusion

14. Claim 41 is not allowed.

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Bekri, et al teach the structure of a gene encoding human ABC-7. US Patent No. 5,858719-A teaches nucleic acid molecules encoding human ATP-binding cassette transport proteins. WO 99/221885 teaches a nucleic acid molecule encoding a human ABC transporter-7.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (703) 305-3008. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned

are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
March 7, 2003

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
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